TPS2671 Poster Session

ARC101-P1-101: A first-in-human phase 1 study of ARC101, a next generation T cell engager (TCE), in patients with advanced solid tumors.

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Background: T-cell Engagers (TCEs) are emerging as a promising immuno-therapeutic modality in the treatment of solid tumors, demonstrating outstanding potency and a manageable safety profile. Claudin 6 (CLDN6) is an oncofetal protein that has recently emerged as a particularly attractive tumor-associated antigen (TAA) for TCE therapy because of its highly tumor-restricted pattern of expression. ARC101 is a bispecific antibody that targets CLDN6 on tumor cells with high specificity and selectivity, and CD3 on T cells. In pre-clinical models, ARC101 demonstrated potent cytolytic activity at low concentrations against a panel of CLDN6-expressing tumor cells in vitro and an ovarian cancer xenograft in vivo. **Methods:** First-in-human, multicenter, phase 1 study ARC101-P1-101 (NCT06672185) aims to determine the optimal dosing, safety, pharmacokinetics (PK), pharmacodynamics (PD), and preliminary antitumor efficacy of ARC101 as monotherapy in patients with locally advanced or metastatic CLDN6 expressing solid tumors. The study will be conducted according to the Bayesian Optimal Interval (BOIN) design in two parts: Part 1 (dose escalation) and Part 2 (dose expansion). Part 1 is designed to select the Maximum Tolerated Dose (MTD), Recommended-Phase 2-Dose (RP2D) and dosing schedule of ARC101. Part 1 will start with an 'Accelerated Titration Phase', with cohorts of at least one, but no more than three patients and a fixed dose, intravenous regimen. Once a single event of clinically significant toxicity of Grade $\geq$2 occurs, the 'Standard Titration Phase' will be initiated with cohorts of at least three patients per ARC101 target dose level. Once immune-related toxicity is observed, the regimen may be changed to a 'Fractionated Step-up Dosing' IV regimen. The study design allows for backfill cohorts and intra-patient dose escalations. Part 2 will further explore the safety, PK/PD characteristics, and preliminary efficacy of ARC101 administered at the RP2D and schedule identified in Part 1 in patients with testicular and ovarian cancer. Key eligibility criteria include patients with any advanced or refractory solid tumor malignancy that expresses CLDN6 and is metastatic or unresectable. Patients must be $\geq$18 years of age and have Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1. Patients must have received standard therapy for advanced or metastatic disease, and disease must be measurable per Response Criteria in Solid Tumors (RECIST) v1.1 or evaluable. Mandatory requirement of a pre-study tumour sample for IHC analysis will facilitate the exploratory objective of biomarker analysis, including correlating CLDN6 expression with treatment response. The study is actively enrolling participants for the dose escalation phase. Contact clinicaltrials@thirdarcbio for additional information. Clinical trial information: NCT06672185. Research Sponsor: None.